Remarks

Prior to this amendment, claims 1-33 and 46-57 were pending in this application. Claims 1-10, 26-33 and 46-54 are currently withdrawn. Claims 12, 13, 20, and 57 are amended and new claims 58 and 59 are added. Claims 10 and 14 are canceled herein without prejudice.

No new matter has been added in this amendment. Unless specifically stated otherwise, none of these amendments are intended to limit the scope of any claim. Applicants reserve the right to pursue any removed subject matter in a related application. After entry of this amendment, **claims 1-9, 11-13, 15-33 and 46-59 are pending** (of which claims 1-9, 26-33, and 46-54 are withdrawn).

Detailed Action

Applicants thank Examiner Leavitt for withdrawing the finality of the March 20, 2008 Office action and entering the Amendment and Response submitted on August 20, 2008. Applicants also thank the Examiner for withdrawing the restriction requirement between Groups III and IV and rejoining claims 23-25 with previously examined claims 11-22 and 55-57.

Priority of claims 19 and 20

Applicants thank Examiner Leavitt for acknowledging that March 12, 2002 is the effective priority date for claim 19 and that claims 55-57 have an effective priority date of May 15, 2002.

Applicants also thank Examiner Leavitt for acknowledging that claim 20 will have an effective priority date of May 15, 2002 if it is amended in the future to be directed to the use of CD40 to induce maturation of dendritic cells only. For ease of prosecution, claim 20 is amended herein to be directed to the use of tumor necrosis factor-α, lipopolysaccharide, CD40 ligand, or phorbol 12-myristate 13-acetate, all of which derive support from U.S. Provisional Application No. 60/380,978, filed May 15, 2002. In addition, new claim 58 is added to be directed to the use of interleukin-4 and granulocyte-macrophage-colony stimulating factor, which derive support

from U.S. Provisional Application No. 60/419,179. As new claim 58 does not encompass an elected species, Applicants submit that claim 58 be withdrawn. New claim 59 is added to be directed to the use of CD40 only.

Withdrawal of Non-Compliant Amendment and Claim Rejections

Applicants thank Examiner Leavitt for withdrawing the Notice of Non-Compliant Amendment under 37 C.F.R. 1.48, as well as the rejections of claims 11-16 and 21-22 under 35 U.S.C. §102(a) and claims 11-19 and 20 under 35 U.S.C. §103.

New Grounds of Rejection

Claim Rejections Under 35 U.S.C. §112, second paragraph

Claims 12 and 14 are rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite. Claim 12 is rejected as the "cell recited in claim 12 appears to already express DDR1. Thus it is unclear the functional role of the agent that induces expression of DDR1 in cells that already express DDR1" (Office action at page 6). Applicants respectfully disagree. However, solely to advance prosecution in this case, claim 12 is amended to recite "with an agent that up-regulates the expression of DDR1." Support for this amendment of claim 12 can be found in the specification at least at page 46, line 25 through page 47, line 11. In view of the amendment of claim 12, Applicants respectfully request that this rejection of claim 12 be withdrawn.

Claim 14 is rejected as "it is unclear how transfection of [the] immature dendritic cell or the immature macrophage with a nucleic acid encoding DDR1b brings about the claimed contacting of the immature dendritic cell or the immature macrophage with the agent that induces expression of DDR1" (Office action at page 7). Applicants respectfully disagree. However, solely to advance prosecution in this case, claim 14 is canceled rendering the rejection of this claim moot.

Claim Rejections Under U.S.C. §103

Claims 11-25, 55, and 57

Claims 11-25, 55, and 57 are rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Radziejewski *et al.* (U.S. Patent No. 6,022,694) in view of Lipford *et al.* (U.S. Published Patent Application No. 2003/0148316). Applicants respectfully disagree.

As stated in the Office action dated March 20, 2008, claims 11-16 and 21-22 (with regard to the term "granulocyte-macrophage-colony stimulating factor") derive support from U.S. Provisional Application No. 60/363,734, filed March 12, 2002. In addition, as discussed above, March 12, 2002 is the effective priority date for claim 19 and the Office acknowledges that May 15, 2002 is the effective priority date for claims 55-57. Claims 17 and 18 derive support from U.S. Provisional Application No. 60/419,179, filed October 16, 2002. Finally, claim 20, as amended herein, and claims 23-25 derive support from U.S. Provisional Application No. 60/380,978, filed May 15, 2002.

Lipford *et al.* discloses that DDR1 (also referred to as Accession No. U48705 and CD167a) is upregulated during immunostimulation with CpG oligonucleotides. Lipford *et al.* also discloses the use of agents, such as antibodies, that simulate dendritic cells. Lipford *et al.* (filed on August 1, 2002) claims the benefit of U.S. Provisional Application No. 60/309,260 and thus has an effective priority date of August 1, 2001. However, Provisional Application No. 60/309,260 does not disclose DDR1 (or Accession No. U48705 or CD167a), nor does it disclose DDR1-activating agents, including antibodies that stimulate or induce dendritic cells. Accordingly, the priority date of Lipford *et al.*, with respect to (i) DDR1, (ii) DDR1-activating agents, and (iii) antibody stimulation of dendritic cells, is August 1, 2002.

Claims 11-16, 19-25, 55, and 57 (directed to the use of a DDR1-activating agent to activate DDR1 and induce the maturation of an immature macrophage or immature dendritic cell) have an effective priority date of March 12, 2002 or May 15, 2002, which predate the August 1, 2002 priority date of Lipford *et al.* Therefore, Lipford *et al.* is improperly cited against claims 11-16, 19-25, 55, and 57. Radziejewski *et al.* discloses the utilization of collagen to support the growth, survival, or differentiation of DDR1-expressing cells. Radziejewski *et al.*

also discloses that COS cells used to express DDR1 were cultured in 10% serum. However, Radziejewski *et al.* does not specifically disclose differentiation of macrophages or dendritic cells expressing DDR1 or the method of inducing the maturation of an immature macrophage or an immature dendritic cell by contacting the cells with a DDR1-activating agent. Thus, Radziejewski *et al.*, on its own, does not render claims 11-16, 19-25, 55, and 57 obvious. In view of the above discussion, withdrawal of this rejection, as it applies to claims 11-16, 19-25, 55, and 57 is respectfully requested.

Claims 17 and 18, directed to the use of a specific DDR1-activating agent (an anti-DDR1 activating antibody) to induce maturation of an immature macrophage or an immature dendritic cell, derive support from U.S. Provisional Application No. 60/419,179, filed October 16, 2002, which is after the August 1, 2002, filing date of Lipford *et al.* However, MPEP §715.07 states that an applicant can establish prior invention of the claimed subject matter by evidencing "conception of the invention prior to the effective date of the reference coupled with due diligence from prior to the reference date to a subsequent (actual) reduction to practice". Attached herewith is a Declaration of Prior Invention Under 37 CFR §1.131 (Declaration) and **Exhibits A and B**. The Declaration and accompanying **Exhibit A** (dated January 9, 2002) demonstrate that the subject matter of claims 17 and 18 was conceived prior to the August 1, 2002 filing date of Lipford *et al.* Specifically, Exhibit A shows that Dr. Yoshimura conceived of the idea to use an anti-DDR1 antibody to activate DDR1 before the reference date (Exhibit A, page 1, paragraph 2). Furthermore, the Declaration and accompanying **Exhibit B** demonstrate that after January 9, 2002, the invention was diligently reduced to practice no later than August 14, 2002 (less than two weeks after the August 1, 2002 reference date). In particular, Exhibit B shows that a DDR1-activating anti-DDR1 antibody was used to (i) change the morphology of polymorphonuclear (PMN) cells (Figure 11) and (ii) increase the release of monocyte chemoattractant protein (MCP-1) from PMN cells (Figure 12). Both morphological changes and secretion of a chemokine, such as MCP-1, are measures of cell maturation.

MPEP §715.02 states that a "reference or activity applied against generic claims may (in most cases) be antedated as to such claims by an affidavit or declaration under 37 CFR 1.131 showing completion of the invention of a single species, within the genus, prior to the effective

date of the reference or activity". Applicants submit that the data presented herewith, evidencing the use of a single anti-DDR1 activating antibody, is sufficient support to antedate Lipford *et al.* because it is representative of the entire genus of anti-DDR1 activating antibodies that specifically bind DDR1. Moreover, "[e]ven if applicant's 37 CFR 1.131 affidavit is not fully commensurate with the rejected claim, the applicant can still overcome the rejection by showing that the differences between the claimed invention and the showing under 37 CFR 1.131 would have been obvious to one of ordinary skill in the art, in view of applicant's 37 CFR 1.131 evidence, prior to the effective date of the reference(s) or the activity. Such evidence is sufficient because applicant's possession of what is shown carries with it possession of variations and adaptations which would have been obvious, at the same time, to one of skill in the art" (MPEP 715.02). Even with regard to unpredictable arts, such as antibodies, Applicants submit that it would have been obvious to one of skill in the art to identify additional anti-DDR1 activating antibodies that specifically bind DDR1, given the identification of the first anti-DDR1 activating antibody, particularly because the antigen (DDR1) was known.

In view of the evidence presented in the Declaration and Exhibits, and the discussion presented above, Applicants submit that they have demonstrated prior invention of the subject matter of claims 17 and 18 vis-à-vis Lipford *et al.* Thus, Lipford *et al.* is not available as prior art. Radziejewski *et al.* discloses anti-DDR1 antibodies, but does not specifically disclose their use to activate DDR1 and induce the maturation of an immature macrophage or an immature dendritic cell. Thus, Radziejewski *et al.*, on its own, does not render claims 17 and 18 obvious. In view of the Declaration of Prior Invention Under 37 C.F.R. §1.131, accompanying Exhibits, and the above arguments, reconsideration and withdrawal of this rejection, as it applies to claims 17 and 18, is respectfully requested.

Claim 56

Claim 56 is rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Radziejewski *et al.*, in view of Lipford *et al.* and Vogel *et al.* (WO 98/34954). Applicants respectfully disagree. As discussed above, claim 56 has an effective priority date of May 15, 2002, which predates the August 1, 2002 filing date of Lipford *et al.* Thus, Lipford *et al.* is improperly cited against claim 56. Neither Radziejewski *et al.,* nor Vogel *et al.* specifically

disclose differentiation of macrophages or dendritic cells expressing DDR1. Thus, the combination of Radziejewski *et al.* and Vogel *et al.* do not render claim 56 obvious. Withdrawal of this rejection of claim 56 is respectfully requested.

Note to Examiner

Applicants' representatives have recently discovered that two published journal articles (Matsuyama *et al.*, *FASEB J.*, Jul;17(10):1286-8. Epub 2003 May 8, 2003 and Matsuyama *et al.*, *J. Immunol.*, Oct 1;171(7):3520-32, 2003), which disclose the subject matter of Examples 2 and 4 of the subject application, respectively, are to be retracted by Inventor Yoshimura. The retraction results from the recent determination that the flow cytometry data described in these articles (and in this application) may be flawed. As the data demonstrating changes in cell surface protein expression levels (specifically, CD11c, CD14, CD40, CD80, CD83, CD86, HLA-DR, MHC Class 1, and CCR7) as a downstream effect of DDR1 activation was presented in this application exclusively using flow cytometric methods, Applicants have amended claim 57 so that it no longer refers to the up-regulation of "cell surface proteins." Applicants do not believe that the retraction of the two journal articles affects the remaining claims pending in this application because those claims are enabled by data generated by methods other than flow cytometry.

Conclusion

Based on the foregoing arguments, the claims are in condition for allowance and notification to this effect is requested. If for any reason the Examiner believes that a telephone conference would expedite allowance of the claims, please telephone the undersigned at the number listed below.

Respectfully submitted,

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